



IN THE UNITED STATES PATENTS AND TRADEMARKS OFFICE

In re: H. SHIMIZU et al.

Examiner: PULLIAM, A

Serial No. 09/600,744

Group: 1615

Filed: July 20, 2000

For: PRODUCTION METHOD FOR SUSTAINED-RELEASE PREPARATION

9/Declaration

11/32

TECH CENTER 1600/2900

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DECLARATION UNDER RULE 132

Honorable Commissioner of Patents and Trademarks, Washington, D. C.

Sir:

I, Mr. Kei Mukai declare:

That I am a citizen of Japan and a resident of 16-4, Kisaichi 2-chome, Katano-shi, Osaka, JAPAN;

That I was born on April 26, 1966 in Hirakata-shi, Osaka, Japan and graduated from the department of Chemical Engineering, Kyoto University, Japan, in March 1992;

That I have been employed by Takeda Chemical Industries, Ltd., Osaka, Japan since April 1992, and have been engaged in research in pharmaceuticals at the Pharmaceutical Development Laboratories of the Pharmaceutical Production Division since 1992;

That I am a member of the Chemical Engineering Society, Japan,;

That I am one of the co-inventors of United States Patent Application Serial No. 09/600,744 and

That I sincerely declare that, under my direction and/or control, the following experimentation was conducted:

Experiment

Experimental Example 1

An ice layer with a thickness of about 2 mm was previously formed on a lyophilizing tray (a width of 290 mm, a length of 445 mm and a depth of 25 mm) at about -30°C using water for injection. The ice layer was also formed on the inner wall of the tray (ice-lining). 82.5 g of mannitol was dissolved in 500 mL of water for injection with cooling at about 5°C. The

solution was added on the lyophilizing tray on which the ice layer had been formed. After thoroughly freezing at about  $-30^{\circ}\text{C}$ , the sample was lyophilized by the conventional method.

An observation of the lyophilized sample after lyophilization revealed that the sample had been scattered.

#### Experimental Example 2

An ice layer with a thickness of about 2 mm was previously formed on a lyophilizing tray (a width of 270 mm, a length of 445 mm and a depth of 35 mm) at about  $-30^{\circ}\text{C}$  using water for injection. The ice layer was also formed on the inner wall of the tray (ice-lining). 130 g of microcapsule powder was dispersed in 500 mL of water for injection with cooling at about  $5^{\circ}\text{C}$ . The suspension was added on the lyophilizing tray on which the ice layer had been formed. After thoroughly freezing at about  $-30^{\circ}\text{C}$ , the sample was lyophilized by the conventional method.

An observation of the lyophilized sample after lyophilization revealed that no scattering had occurred:

It is declared by the undersigned that all statements made herein of my own knowledge are true and that all statements made on information are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Signed this on October 15, 2001

Kei Mukai

Kei MUKAI